(11) (A) No. 999238

(45) ISSUED 761102

(52) CLASS 167-316
C.R. CL.

(19) (CA)

CANADIAN PATENT

(54) ORAL OR DENTAL PREPARATION

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(21) APPLICATION No. 203,877
(22) FILED 740703
DIV'N OF APPL'N No. 176,790 filed 730718

(30) PRIORITY DATE

No. OF CLAIMS 11 - No drawing

ABSTRACT OF DISCLOSURE

An oral or dental preparation containing hydroxyapatite. The preparation may be in the form of a toothpaste, tooth powder chewing tablet, chewing lozenge, gum ointment, mouthwash, mouthwash or mouthbath concentrates or gargles. They can contain also an osmotically active inorganic salt combination, a local anaesthetic, silicic acid, a foaming agent and allantoin. The preparations are usual in improving dental and oral hygiene.

This invention relates to oral and dental preparations in all the various forms suitable for oral hygiene such as toothpastes, mouthwashes, mouthwash concentrates, gargles, chewing gum, chewing tablets or lozenges for oral and dental hygiene as well as creams and ointments for the gums. These preparations according to the invention contain extremely finely divided hydroxy apatite for remineralizing the enamel and preferably also a special inorganic salt combination and a local anaesthetic.

It is known that a high proportion of the population with teeth, estimated by the dental profession to amount to 20 to 25%, suffers from hypersensitivity or hyperaesthesia of the teeth, in other words pain in response to mechanical, chemical and thermal stimuli, without any visible dental diseases such as caries which would require dental treatment.

In addition to this section of the population, many people suffer from chronic bleeding of the gums, a consequence of gingivitis, deposits of secretions from the gingival crevices and lesions in the bed of the teeth, which in advanced stages result in loosening or loss of teeth and in loss of the tooth bed.

Anaerobic putrefactive bacteria which cause halitosis are able to multiply rapidly in the protective environment of the inflamed and secretion-depositing tissue so that they easily give rise to inflammation of the buccal mucous membrane and even irritation of the pharyngeal cavity.

Since the treatment of these lesions of the teeth and mouth take up a great deal of the dentist's time, it is

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an object of this invention to provide the patient with effective means of permanently treating these conditions in the course of his normal routine of dental hygiene.

The hypersensitivity of the teeth occurs mainly at the neck of the teeth when the soft dentine becomes exposed between the boundary of the enamel and the gum line due to recession of the gums. The action of lactic acid forming lactobacilli or the mechanical action of braces (even in children) or the engaging parts of dentures during chewing may also damage the protective enamel so that the dentinal canaliculi which are then exposed transmit every mechanical, chemical or thermal irritation as a painful stimulus to the tooth pulp.

According to the invention, the dentinal canaliculi can be effectively sealed by applying an inorganic remineralizing layer which chemically very closely resembles the composition of the enamel and dentine so that the pain reflex can no longer reach the pulp.

It is known that repeated treatment with inorganic salts, particularly sodium bicarbonate, sodium chloride or strontium chloride at high concentrations in the presence of glycerine desensitizes the sensitive parts of the teeth but that this desensitization is reversible so that pain is again felt soon after therapy has stopped.

It is an object of this invention to replace this temporary desensitization by a long lasting remineralization.

It has been found that an alkaline earth metal phosphate which is chemically analogous to dental enamel and dentine, namely hydroxy apatite having the chemical formula:

$$C_5 (PO_4)_3 OH \quad \text{or} \quad 3\, Ca_3 (PO_4)_2 \cdot Ca (OH)_2$$

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and the composition:

P_2O_5 : 40 - 41%

CaO : 52 - 54%

applied in a finely divided form is suitable for deposition in the dentinal canaliculi. The average particle size of the hydroxy apatite is preferably smaller than 10 µ and in particular in the region of about 6 to 8 µ. At least 50% by weight and preferably at least 75% by weight of the particles of hydroxy apatite should be within this range of particle sizes. The bulk weight of the hydroxy apatite is preferably less than 180 g/l, e.g. about 150 g/l.

If this finely divided hydroxy apatite is repeatedly brought into contact with sensitive teeth over a prolonged period of time, for example when cleaning the teeth or when chewing tablets or chewing gum, then it diffuses into the exposed dentinal canaliculi by virtue of its very slight solubility in water and saliva due to hydrolysis and becomes deposited in the microscopically fine cavities left in the hydroxy apatite structure which has been formed in the organic matrix. The dentinal canaliculi are gradually sealed and permanent relief from pain is obtained.

It has surprisingly been shown that it is precisely this very finely divided hydroxy apatite which can rapidly and permanently seal the dentinal canaliculi and so bring permanent relief from pain. Other very finely divided materials, even those which are chemically very similar such as calcium carbonate which is free from hydroxyl groups do not have a comparable effect of permanently relieving pain by remineralizing the structure of the teeth. The choice of hydroxy apatite therefore constitutes an essential element

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of the invention.

The preferred quantity in which this finely divided hydroxy apatite is used is 5 to 40%, preferably 8 to 20%, in toothpaste formulations, 60 to 90%, preferably 70 to 80%, in chewing tablets, 5 to 30%, preferably 10 to 20%, in chewing gum, 30 to 60%, preferably 30 to 45%, in tooth powder, and 10 to 30%, preferably 12 to 18%, in creams and ointments applied to the margin of the gum, the percentages being based in each case on the total preparation. All the percentages indicated are percentages by weight both in the above cases and in the figures given hereinafter.

Since patients suffering from this hyperaesthesia feel pain even with the slightest contact, even when applying toothpaste or using mouthwashes or when chewing, the preparations according to the invention may contain a surface anaesthetic, e.g. the well-known anaesthetic benzocaine, p-aminobenzoic acid ethyl ester, e.g. at a concentration of 0.05 - 5%, preferably 0.1 to 0.5%. Since benzocaine, is only very sparingly soluble in water, its action is restricted locally to the surface of the mucous membranes. Its uniform and rapid distribution is achieved by dissolving the dry substance in a small quantity of alcohol (1-10% based on the total quantity) and by adding physiologically harmless surface active agents to assist the wetting effect.

All the oral preparations according to the invention preferably also contain an inorganic salt combination which has an osmotic action on the gum and buccal mucous membrane. This salt combination consists in particular of a mixture of sodium bicarbonate, sodium chloride, potassium sulphate and magnesium carbonate or magnesium chloride. The

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complete preparation preferably contains the salt mixture in quantities of 2 to 35%, the proportion of sodium bicarbonate amounting to 60 to 80% of all the salts in the combination.

Such a salt combination has a powerful osmotic action on the inflamed gums and mucous membranes. The inflamed gums are thoroughly dehydrated and tightened, and tough tooth deposits and secretions from the gingival crevices are lifted from their supports, particularly by the high concentration of sodium bicarbonate present, and thus easily removed. The mucous membranes now freed from the deposits of necrotic cell layers and excess tissue serum again receive a plentiful blood supply and are able to heal. Bleeding of the gums, the external sign of increased tissue pressure due to accumulation of serum, automatically ceases when the tissue is relieved and the gum regains its healthy, pale pink colour.

Allantoin may also be added in amounts of 0.01 to 0.5%, preferably 0.05 to 0.1%, for rapid regeneration of the healing mucous membranes and gums.

The preparations according to the invention may also contain any of the usual additives. Toothpastes and powders may contain all the dentifricial cleaning substances, aromatic and flavouring substances, foaming substances and substances which have a brightening action on the teeth. A mild polishing agent may be added, e.g. colloidal silicic acid, preferably having a particle size of about 10 mu. Foaming agents which are compatible with the mucous membranes may be added, e.g. in quantities of 0.1 to 12%, preferably 0.5 to 4%. Chewing gum, chewing tablets and lozenges contain the additives according to the invention incorporated in the usual vehicles. Vehicle mixtures which are free from sugar may be preferred.

The invention will now be described in more detail with the aid of the following examples but is not restricted to them.

All the figures given in the following formulations are in grams.

Example 1

Toothpaste	A	B
Amorphous hydroxy apatite (average particle size 6-8 μ)	9.000	15.000
p-Aminobenzoic acid ethyl ester	0.125	0.250
Alcohol (ethanol/propanol)	2.375	2.250
Colloidal silicic acid	2.800	2.800
Magnesium carbonate	1.250	1.500
Sodium chloride	0.175	0.200
Potassium sulphate	0.175	0.200
Sodium bicarbonate	6.250	6.400
Glycerol (86%)	24.000	10.000
Sorbitol (70%)	--	15.000
Sodium p-hydroxybenzoic acid ethyl ester	0.200	0.200
Sodium lauryl sulphate	2.750	2.750
Sodium oleic acid methyl taurine	0.900	0.900
Carboxymethylcellulose	1.250	1.000
Titanium dioxide	0.750	--
Flavouring and optionally colouring	1.500	1.300
Sodium saccharine	0.250	0.250
Deionised water	46.050	39.800
Allantoin	0.100	0.100
1,3-bis -(β-ethylhexyl)-5-methyl-5-amino-hexahydropyrimidine	0.100	0.100
	100.000	100.000

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Example 2

Tooth powder, readily pourable, not forming lumps when stored and not separating when shaken in transport

	A	B
Amorphous hydroxy apatite (average particle size 6-8 µ)	36.000	42.000
p-Aminobenzoic acid ethyl ester	0.500	0.300
Colloidal silicic acid	12.000	6.000
Sodium bicarbonate	25.000	25.300
Sodium chloride	0.700	0.700
Magnesium carbonate	5.000	5.000
Potassium sulphate	0.700	0.700
Sodium lauryl sulphate	11.000	10.000
Sodium oleic acid methyl taurine	3.600	4.600
Sodium saccharine	1.000	0.800
Sodium p-hydroxybenzoic acid methyl ester	0.100	0.100
Flavouring	4.300	4.500
1,3-bis-(β-ethylhexyl)-5-methyl-5-amino-hexahydropyrimidine	0.100	--
	100.000	100.000

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Example 3

Chewing Tablet for tooth cleaning

	A	B
Amorphous hydroxy apatite (average particle size 6-8 µ)	73.050	73.200
p-Aminobenzoic acid ethyl ester	0.150	0.150
Alcohol (ethanol/propanol)	3.000	3.000
Pulverulent polyvinyl pyrrolidone	2.500	2.500
Carboxymethylcellulose	1.500	1.450
Starch	2.400	2.000
Allantoin	0.100	0.050
Sodium lauryl sulphate	0.500	0.500
Sodium bicarbonate	12.500	12.500
Magnesium carbonate	2.500	2.500
Sodium chloride	0.350	0.350
Potassium sulphate	0.350	0.350
Flavouring	1.000	1.100
Sodium saccharine	0.100	0.150
L-malic acid (to prevent the formation of tartar)	--	0.200
	100.000	100.000

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Example 4

Chewing gum for tooth cleaning

The basic substances used for the chewing gum are known trade products and do not constitute part of the invention. The preparation should preferably be free from sugar since it is well known that the slow consumption of substances containing sugar has a powerful cariogenic effect.

	A	B	C	D	E	F
		with sugar			without sugar	
Chewing gum base	20.00	18.00	21.00	22.00	24.00	20.00
Sugar	30.00	25.00	35.00	-	-	-
Corn syrup	19.00	21.00	16.00	-	-	-
Mannitol	7.90	17.60	5.70	34.20	34.10	32.00
Sorbitol	-	-	-	22.45	21.45	24.20
Sodium saccharine	0.10	0.10	0.10	0.10	0.10	0.10
Sodium cyclamate	-	-	-	0.30	0.30	0.30
86% glycerol	0.25	0.25	0.30	1.80	2.00	1.50
Amorphous hydroxy-apatite average particle size 6-8 µ	10.00	9.00	12.00	10.00	9.00	12.00
p-Aminobenzoic acid ethyl ester	0.10	0.10	0.10	0.10	0.10	0.10
Sodium bicarbonate	6.30	6.20	6.50	6.30	6.20	6.50
Magnesium carbonate	1.30	1.20	1.50	1.30	1.20	1.50
Sodium chloride	0.20	0.20	0.20	0.20	0.20	0.20
Potassium sulphate	0.20	0.20	0.20	0.20	0.20	0.20
Allantoin	0.05	0.05	0.10	0.05	0.05	0.10
L-malic acid	-	-	0.30	-	-	0.30
Flavouring	1.00	1.00	1.00	1.00	1.00	1.00
1,3-bis-(β-ethylhexyl) -5-methyl-5-amino-hexahydropyrimidine	-	0.10	-	-	0.10	-
	100.00	100.00	100.00	100.00	100.00	100.00

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Example 5

Ointment for application to the gum margin

Amorphous hydroxy apatite	15.000	16.000
Colloidal silicic acid	4.000	3.500
99.5% glycerol	67.875	67.775
Carboxymethylcellulose	3.000	2.800
Sodium bicarbonate	6.450	6.250
Magnesium carbonate	1.250	1.250
Potassium sulphate	0.175	0.175
Sodium chloride	0.175	0.175
Sodium saccharine	0.250	0.200
p-aminobenzoic acid ethyl ester	0.125	0.125
p-hydroxybenzoic acid propyl ester	0.100	0.100
p-hydroxybenzoic acid propyl ester	0.100	0.100
Sodium oleic acid methyl taurine	0.500	0.500
1,3-bis-(β-ethylhexyl)-5-amino-hexahydrophyrimidine	-	0.050
Flavouring	1.000	1.000
	100.000	100.000

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THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. An oral or dental preparation containing 5 to 90% by weight of finely divided hydroxy apatite having an average particle size of less than 10μ.

2. A preparation according to claim 1, wherein the hydroxy apatite is amorphous.

3. A preparation according to claim 1 or 2, also including 2 to 35% by weight of an osmotically active inorganic salt combination comprising sodium bicarbonate, sodium chloride, magnesium carbonate, or magnesium chloride and potassium sulfate, the sodium bicarbonate constituting 60% to 80% by weight of the total salt combination.

4. A preparation according to claim 1 or 2, also including 0.05 to 5% by weight of a local anaesthetic.

5. Oral and dental preparations in the form of toothpaste, tooth powder, chewing tablet or lozenge, chewing gum for oral and dental hygiene, ointment for the gums, mouthwash, mouthwash and mouth bath concentrates and gargles, containing (1) 5 to 90% by weight of finely divided hydroxy apatite having an average particle size of less than 10μ (2) 2 to 35% by weight of an osmotically active inorganic salt combination comprising sodium bicarbonate, sodium chloride, magnesium carbonate, or magnesium chloride and potassium sulfate, the sodium bicarbonate constituting 60% to 80% by weight of the total salt combination and (3) 0.05 to 5% by weight of a local anaesthetic.

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6. A preparation according to claim 5, in which the local anaesthetic is p-aminobenzoic acid ethyl ester.

7. A preparation as claimed in claim 5 in which the hydroxy apatite has an average particle size of 6 to 8μ and a bulk weight of about 150 g/l.

8. A preparation according to claim 5, also including colloidal silicic acid as a polishing agent.

9. A preparation according to claim 5, also including a foaming agent compatible with the mucous membrane.

10. A preparation according to claim 5, also including allentoin in an amount of 0.01 to 0.5% by weight.

11. An oral or dental preparation in the form of toothpaste, tooth powder, chewing tablet or lozenge or chewing gum for oral or dental hygiene or ointments for the gums, comprising hydroxy apatite having an average particle size of from 6 to 8μ with a bulk weight of about 150 g/l, a local anaesthetic which is p-aminobenzoic acid ethyl ester and is present in an amount of 0.05 to 5.0% of the total preparation, an osmotically active inorganic salt combination which consists of sodium bicarbonate, sodium chloride, magnesium carbonate or magnesium chloride and potassium sulphate, the sodium bicarbonate constituting 60 to 80% of the total salt combination and the quantity of this salt combination being from 2 to 35% of the total preparation, colloidal silicic acid with an average particle size of 10 mμ, a foaming agent compatible with the mucous membrane in an amount of from 0.1 to 12% of the total preparation, and allantoin in an amount of from 0.01 to 0.5% of the total preparation.

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SUBSTITUTE

REMPLACEMENT

SECTION is not Present

Cette Section est Absente